

DOCKET NO. 329368-101A

SERIAL NO. 08/854,825

1' said [polypeptide] selected CTL epitope is DLMGYIPLV (Core<sub>132-140</sub>; SEQ ID NO:54), then said molecule comprises at most nine amino acids.

2  
2' 52. (Twice Amended) A method of stimulating a cytotoxic T-lymphocyte (CTL) response to an hepatitis C viral immunogen, comprising contacting an HLA class I-restricted cytotoxic T lymphocyte with a composition comprising a peptide that induces an hepatitis C virus (HCV)-specific response in cytotoxic T lymphocytes [having] comprising a sequence that has no more than a total of two single amino acid substitutions, deletions or insertions at the corresponding positions as in a CTL epitope which is ADLMGYIPLV (Core<sub>131-140</sub>; SEQ ID NO:1), LLALLSCLTV (Core<sub>178-187</sub>; SEQ ID NO:2), QLRRHIDLLV (E1<sub>257-266</sub>; SEQ ID NO:3), KLVALGINAV (NS3<sub>1406-1415</sub>; SEQ ID NO:28), or LLFNILGGWV (NS4<sub>1807-1816</sub>; SEQ ID NO:35) or has no more than a total of one single amino acid substitution, deletion or insertion at the corresponding amino acid positions as in a CTL epitope which is ADLMGYIPLV (Core<sub>131-140</sub>; SEQ ID NO:1), DLMGYIPLV (Core<sub>132-140</sub>; SEQ ID NO:54), LLCPAGHAV (NS3<sub>1169-1177</sub>; SEQ ID NO:26), SLMAFTAAV (NS4<sub>1789-1797</sub>; SEQ ID NO:34), or ILDSFDPLV (NS5<sub>2252-2260</sub>; SEQ ID NO:42).

3  
3' 56. (Twice Amended) A method of detecting cytotoxic T cells that respond to a T cell epitope of hepatitis C virus (HCV), the method comprising the steps of:  
(a) preparing HLA class I-restricted cytotoxic T cells;  
(b) preparing HLA class-I matched and -mismatched target cells;  
(c) containing separately matched and mismatched target cells with a composition comprising a peptide that induces an HCV-specific response in cytotoxic T lymphocytes having the sequence that has no more than a total of two single amino acid substitutions, deletions or insertions at the corresponding positions as in a CTL epitope which is ADLMGYIPLV (Core<sub>131-140</sub>; SEQ ID NO:1), LLALLSCLTV (Core<sub>178-187</sub>; SEQ ID NO:2), QLRRHIDLLV (E1<sub>257-266</sub>; SEQ ID NO:3), KLVALGINAV (NS3<sub>1406-1415</sub>; SEQ ID NO:28), or LLFNILGGWV (NS4<sub>1807-1816</sub>; SEQ ID NO:35) or has no more than a total of one single amino acid substitution, deletion or insertion at the corresponding amino acid positions as in a CTL epitope which is DLMGYIPLV

DOCKET NO. 329368-101A  
SERIAL NO. 08/854,825

73 (Core<sub>132-140</sub>; SEQ ID NO:54), LLCPAGHAV (NS<sub>31169-1177</sub>; SEQ ID NO:26), SLMAFTAAV (NS<sub>41789-1797</sub>; SEQ ID NO:34), or ILDSFDPLV (NS<sub>52252-2260</sub>; SEQ ID NO:42);

(d) combining the cytotoxic T cells separately with the matched and mismatched target cells; and

(e) measuring cytolysis.

58. (Twice Amended) A pharmaceutical composition comprising a peptide that induces an hepatitis C virus (HCV)-specific response in cytotoxic T lymphocytes having a sequence that has no more than a total of two single amino acid substitutions, deletions or insertions at the corresponding positions as in a CTL epitope which is ADLMGYIPLV (Core<sub>131-140</sub>; SEQ ID NO:1), LLALLSCLTV (Core<sub>178-187</sub>; SEQ ID NO:2), QLRRHIDLLV (E1<sub>257-266</sub>; SEQ ID NO:3), KLVALGINAV (NS<sub>31406-1415</sub>; SEQ ID NO:28), or LLFNILGGWV (NS<sub>41807-1816</sub>; SEQ ID NO:35) or has no more than a total of one single amino acid substitution, deletion or insertion at the corresponding amino acid positions as in a CTL epitope which is DLMGYIPLV (Core<sub>132-140</sub>; SEQ ID NO:54), LLCPAGHAV (NS<sub>31169-1177</sub>; SEQ ID NO:26), SLMAFTAAV (NS<sub>41789-1797</sub>; SEQ ID NO:34), or ILDSFDPLV (NS<sub>52252-2260</sub>; SEQ ID NO:42), and a pharmaceutically acceptable carrier.

60. (Amended) A conjugate comprising

4556 (a) a molecule which comprises:

a polypeptide having no more than a total of two single amino acid substitutions, deletions or insertions at the corresponding positions as in a CTL epitope which is ADLMGYIPLV (Core<sub>131-140</sub>; SEQ ID NO:1), LLALLSCLTV (Core<sub>178-187</sub>; SEQ ID NO:2), QLRRHIDLLV (E1<sub>257-266</sub>; SEQ ID NO:3), KLVALGINAV (NS<sub>31406-1415</sub>; SEQ ID NO:28), LLFNILGGWV (NS<sub>41807-1816</sub>; SEQ ID NO:35) or has no more than a total of one single amino acid substitution, deletion or insertion at the corresponding amino acid positions as in a CTL epitope which is DLMGYIPLV (Core<sub>132-140</sub>; SEQ ID NO:54), LLCPAGHAV (NS<sub>31169-1177</sub>;

DOCKET NO. 329368-101A

SERIAL NO. 08/854,825

SEQ ID NO:26), SLMAFTAAV (NS4<sub>1789-1797</sub>; SEQ ID NO:34), or  
ILDSFDPLV (NS5<sub>2252-2260</sub>; SEQ ID NO:42),; and

(b) a substance selected from the group consisting of a radiolabel, an enzyme, a fluorescent label, a solid matrix, a carrier and an additional molecule of (a).

62. (Amended) A conjugate of claim 60 comprising two molecules, each comprising: a polypeptide no more than a total of two single amino acid substitutions, deletions or insertions at the corresponding positions as in a CTL epitope which is ADLMGYIPLV (Core<sub>131-140</sub>; SEQ ID NO:1), LLALLSCLTV (Core<sub>178-187</sub>; SEQ ID NO:2), QLRRHIDLLV (E1<sub>257-266</sub>; SEQ ID NO:3), KLVALGINAV (NS3<sub>1406-1415</sub>; SEQ ID NO:28), LLFNILGGWV (NS4<sub>1807-1816</sub>; SEQ ID NO:35) or has no more than a total of one single amino acid substitution, deletion or insertion at the corresponding amino acid positions as in a CTL epitope which is DLMGYIPLV (Core<sub>132-140</sub>; SEQ ID NO:54), LLCPAGHAV (NS3<sub>1169-1177</sub>; SEQ ID NO:26), SLMAFTAAV (NS4<sub>1789-1797</sub>; SEQ ID NO:34), or ILDSFDPLV (NS5<sub>2252-2260</sub>; SEQ ID NO:42) [,].

Please enter the following new claims:

65. (New) An isolated molecule comprising a polypeptide that induces an hepatitis C virus (HCV)-specific response in cytotoxic T lymphocytes having a sequence that has

(a) no more than a total of two single amino acid substitutions, deletions or insertions at the corresponding amino acid positions in a CTL epitope which is LLALLSCLTV (Core<sub>178-187</sub>; SEQ ID NO:2), QLRRHIDLLV (E1<sub>257-266</sub>; SEQ ID NO:3), KLVALGINAV (NS3<sub>1406-1415</sub>; SEQ ID NO:28), or LLFNILGGWV (NS4<sub>1807-1816</sub>; SEQ ID NO:35), or

(b) has no more than one single amino acid substitution, deletion or insertion at the corresponding amino acid positions as in a CTL epitope which is ADLMGYIPLV (Core<sub>131-140</sub>; SEQ ID NO:1), DLMGYIPLV (Core<sub>132-140</sub>; SEQ ID NO:54), LLCPAGHAV (NS3<sub>1169-1177</sub>; SEQ ID NO:26), SLMAFTAAV (NS4<sub>1789-1797</sub>; SEQ ID NO:34), or ILDSFDPLV (NS5<sub>2252-2260</sub>; SEQ ID NO:42),